REMARKS

Reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 1-8 are in this case. Claims 1, 3 and 4 have been amended.

35 U.S.C. § 112, 1st Paragraph, Rejections

The Examiner has rejected claims 1-8 under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiners rejections are respectfully traversed.

The Examiner states that although the instant specification is enabling for a method of treating cell lines established from samples of cystic fibrosis (CF) patient resulting from an abnormal expression vector to produce a specific alternative splicing factor (ASF) such as hnRNP A1 or E4-ORF6, it does not reasonably provide enablement for a method of treating an individual suffering from a disease resulting in aberrant splicing in cells due to a mutation leading to exon inclusion, exon skipping or both exon inclusion and exon skipping, comprising administering to the cells or to tissue or organs of the individual an ASF, whereby the abnormal expression shifts towards normal expression of the gene, wherein the disease and the mutation are not defined, and the ASF is not identified. In particular, the Examiner states that there are no indicia that the present application enables the full scope in view of a method for treating a disease resulting form aberrant splicing in cells, and that it requires undue experimentation to assess the effect of an ASF in treating a disease resulting form aberrant splicing in cells.

The present invention is of a method and pharmaceutical compounds for treatment of individuals suffering from a disease resulting from aberrant slicing in expression of a gene, such as cystic fibrosis, by administering an alternative splicing factor (ASF), thereby remedying the aberrant splicing and shifting the expression of the gene to normal expression. While reducing the present invention to practice, the Applicants demonstrated accurate "normal" splicing of affected CFTR gene products by cotransfection of COS cells with recombinant exogenous splicing factors (Example 4), and remedy of aberrant splicing of CFTR transcripts in cells of cystic fibrosis patients by expression of recombinant exogenous splicing factors (Example

5). Thus, Applicants have provided evidence of the efficacy of the method and pharmaceutical compositions of the present invention in remedying the underlying genetic pathology of cystic fibrosis, a commonly used model for genetic diseases of aberrant splicing.

Further, the efficacy of in-vitro models for methods of in-vivo treatment is well known in the art, as evidenced by the numerous references presented in the Response to Official Action dated September 22, 2003. Methods of treatment suitable for use with the methods and pharmaceutical compositions of the present invention are disclosed in the instant specification:

"The ASF may be administered to the cells in any manner known in the art.

By one alternative, a nucleic acid sequence expressing the ASF may be inserted in an expression vector, such as a plasmid containing the coding region for the ASF under control of a suitable expression control element (such as a suitable promoter). Then, said cells of the individual are transfected with said expression vector in order to produce the ASF...The expression vectors may be targeted to the desired cells or to the tissue or organ comprising the cells by any means known in the art for targeting compounds to specific tissue. For example, they may be administered directly to the cells. Where ...the target cells or organs are the lungs, the expression vectors may be present within a carrier suitable for inhaling and penetrating the lungs.

By another alternative, the expression vector may be attached to targeting moiety, such as, for example, a suitable antibody or a ligand of a specific receptor which can specifically bind to the membranes of the desired cells and thus the expression vector to the desired cell population, or to the organ or tissue comprising said cell population. In such a case, the expression vector may be administered systemically, and the targeting moiety ensures that it reaches its proper target cell population.

By yet another alternative, the ASF may be administered as the protein product itself. For example, where the ASF is a protein, it may be administered as a protein, for example inside a suitable vehicle suitable for administration of proteins either by direct administration to the cells, tissue or organ as mentioned above

(inhalation to lungs, injection to the organ, etc.), or alternatively by conjugating the vehicle, to a targeting moiety as described above."(pages 6-7).

Thus, it is Applicants strong opinion that, contrary to the Examiner's assertions, one of ordinary skill in the art, in possession of the teachings of the present invention would be able to use the methods and pharmaceutical compositions of the present invention for treatment of diseases of aberrant splicing by administration of alternative splicing factors (ASF) without undue experimentation, and with a reasonable expectation of success.

35 U.S.C. § 112, 2nd Paragraph, Rejections

The Examiner has rejected claims 1-8 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter which applicants regard as the invention. The Examiner's rejections are respectfully traversed. Claims 1, 3 and 4 have now been amended.

The Examiner has stated that the term "a mutation" in claim 1 renders the claim indefinite. Claim 1 has now been amended, and now recites: "...a disease resulting from aberrant splicing in cells due to either exon inclusion, exon skipping, or both exon inclusion and exon skipping..." thus overcoming the Examiner's rejection.

Regarding claims 3 and 4, the Examiner has stated that the claims are indefinite because they recite a mutation of "3849+10kB C->T" or "5T allele", without identifying the gene having the mutation. Claims 3 and 4 have now been amended to include the term "of the CFTR gene", thereby overcoming the rejections thereof. Support for such an amendment can be found throughout the instant specification (see, for example, page 4, paragraph 0018).

In view of the abovementioned amendments, Applicant believes to have overcome the 35 USC 112, second paragraph rejections.

In view of the above amendments and remarks it is respectfully submitted that claims 1-8 are now in condition for allowance. Prompt notice of allowance is respectfully and earnestly solicited.

Respectfully submitted,

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Date: November 18, 2004.

Enc: Three month's extension fee